REMARKS

Applicants appreciate Examiner's determination that Claims 2-4, 10-21 and 27 are allowable.

Claims 24-26 were rejected under 35 USC §112, first paragraph, as lacking enablement. Claims 1, 6, 8, 22 and 28-29 were rejected under 35 USC §102(b) as being anticipated by Giraldi et al. US 3,074,943. Claims 1, 5-8, 22 and 28-29 were rejected under 35 USC §102(b) as being anticipated by Cutler et al. US 3,097,205. Claims 1, 6, 23 and 28-29 were rejected under 35 USC §102(b) as being anticipated by Cutler et al. US 3,209,003. Claims 1, 6, and 8-9 were rejected under 35 USC §103(a) as being unpatentable over Newton et al. US 5,062,882. Claims 1 and 6 were rejected under 35 USC §103(a) as being unpatentable over Riebel et al. US 6,284,710.

Claims 24-26 were rejected under 35 USC §112, first paragraph, as lacking enablement for the described indications. Specifically the Examiner astates that the specification does not provide enablement for treating all the diseases embraced in the claim language. In addition to the effect of kinase inhibition on angiogenesis, the literature correlating kinase inhibition and disease state modification is vast. Representative examples are described below and submitted in a separate Supplemental Infvention Disclosure Statement.

	Kinase	disease	references
1.	**EGFR-1**	**polycystic kidney disease**	Sweeney, et al., Kidney Int., 57, 33-40 (2000)
		Cancer	Raymond, et al., Drugs, 60, S1, 15-23 (2000)
2.	**IGFR-1**	**cancers**	Khandwala et al., Endocrine Rev., 21(3) 215-244 (2000).
3.	**MET-1**	**cancer**	Cao et al., Proc. Nat. Acad. Sci., USA, 98(13), 7443-7448 (2001)
4.	**LCK-1**	**autoimmune disease**	Kamens, et al., Curr. Opin. in Invest. Drugs 2(9), 1213-1219 (2001).
5.	**PDGFRB-1**	**leukemia**	Scheijen and Griffin, Oncogene, 21, 3314-3333 (2002)
6.	**TEK-1**	**myeloproliferative disorders**	Muller, et al., Leukemia Res., 26, 163-168 (2002)
7.	**ERBB2-2**	**breast cancer**	Artega et al., Sem in Onc., 29, (s11), 4-10 (2002)

The compounds of the present invention have inhibition of the above kinases as described in the specification in Tables 2-5, pages 296-353. Applicants request reconsideration of the 35 USC §112 rejections in view of the above discussion.

Claims 1, 6, 8, 22 and 28-29 were rejected under 35 USC §102(b) as being anticipated by Giraldi et al. US 3,074,943. Applicants request reconsideration of the rejection in view of the amended proviso language in Claim 1 which eliminates compounds of Giraldi et al.

Claims 1, 5-8, 22 and 28-29 were rejected under 35 USC §102(b) as being anticipated by Cutler et al. US 3,097,205. Applicants request reconsideration of the rejection in view of the amended proviso language in Claim 1 which eliminate the compounds of Cutler et al.

Claims 1, 6, 23 and 28-29 were rejected under 35 USC §102(b) as being anticipated by Cutler et al. US 3,209,003. Applicants request reconsideration of the rejection in view of the amended proviso language in Claim 1 which eliminate compounds of Cutler et al.

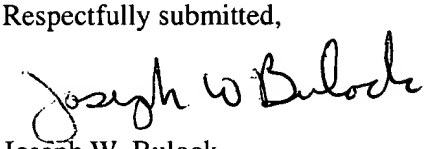
Claims 1, 6 and 8-9 were rejected under 35 USC §103(a) as being unpatentable over Newton et al. US 5,062,882. Newton describes tri-substituted triazines as herbicides (weed killers). The pattern of preferences established by this reference teaches away from the compounds of the current invention. Of the seventy two examples of substituted triazines identified in Newton, only examples 8-9, and 46 did not have di-alkoxy substitution. The biological data described in Table 3 indicates that there was a substantial decrease in activity when R^1 is not methoxy (Examples 8-9) compared with the other compounds. Thus, one skilled in the art would be taught away form the compounds of the present invention. Applicants contend that Newton et al. do not render obvious the disubstituted triazines of the present invention.

Claims 1, and 6 were rejected under 35 USC §103(a) as being unpatentable over Riebel et al. US 6,284,710. Riebel et al. describe triazines as herbicides (weed killers). The compounds of Riebel require the presence of a $-NH_2$ substitutent. Most of compounds made by Riebel and all the compounds tested additionally have haloalkyl or methylthio substitutution on the triazine. This indicates that the "Z-substituent" was important for controlling non-specific toxicity, and that haloalkyl and methylthio substitutents were most preferred "Z-substituents". Thus Riebel et al. teach away from the disubstituted triazines of the present invention which do not have $-NH_2$, haloalkyl or alkylthio substitution on the triazine ring. Applicants contend that the '710 patent does not render obvious the disubstituted triazines of the present invention.

In view of the above, none of the references, taken singly or in any combination, describes or suggests compounds of the present invention. Applicants therefore submit that the compounds of the present invention are not obvious in view of the cited prior art.

It is therefore respectfully submitted that Claims 1-29 are now in condition for allowance. Accordingly, allowance of Claims 1-29 are respectfully solicited.

Respectfully submitted,



Joseph W. Bulock
Attorney for Applicant
Registration No.: 37,103
Phone: 805.447.7966
Date: February 5, 2003

Please send all future correspondence to:
US Patent Operations/ JWBcb
Dept. 430, M/S 27-4-A
AMGEN INC.
One Amgen Center Drive
Thousand Oaks, California 91320-1799

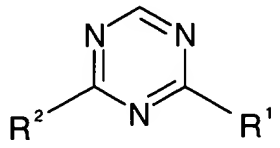
VERSION WITH MARKINGS TO SHOW CHANGES

In the Claims

Cancel claims 8-9, without prejudice.

Amend Claims 1, as follows:

1. (Amended twice) A compound having the formula:



wherein,

Each R^1 and R^2 is independently R^3; R^8; NHR^3; NHR^5; NHR^6; NR^5R^5; NR^5R^6; **[SR^5; SR^6; SR^3; OR^5; OR^6; OR^3; $C(O)R^3$]**; heterocyclyl optionally substituted with 1-4 independent R^4 on each ring; or C1-C10 alkyl substituted with 1-4 independent R^4;

Each R^3 is independently aryl; phenyl optionally substituted with 1-5 independent R^4 on each ring; or heteroaryl optionally substituted with 1-4 independent R^4 on each ring;

Each n is independently 1 or 2;

Each m is independently 0, 1, 2, 3, or 4;

Each R^4 is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8; halo; haloalkyl; SR^5; OR^5; $OC(O)R^5$; NR^5R^5; NR^5R^6; NR^5R^{16}; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)C(O)R^5$; $C(O)NR^5R^5$; $S(O)_nR^5$; $S(O)_nNR^5R^5$; $NR^5C(O)NR^5R^5$; $NR^5C(O)C(O)R^5$; $NR^5C(O)R^5$; $NR^5(COOR^5)$; $NR^5C(O)R^8$; $NR^5S(O)_nNR^5R^5$; $NR^5S(O)_nR^5$; $NR^5S(O)_nR^8$; $NR^5C(O)C(O)NR^5R^5$; $NR^5C(O)C(O)NR^5R^6$; $OC(O)NR^5R^5$; $OS(O)_nNR^5R^5$; $NR^5S(O)_nOR^5$; $P(O)(OR^5)_2$; C1-C10 alkyl substituted with 1-3 independent aryl, R^7 or R^8; or C2-C10 alkenyl substituted with 1-3 independent aryl, R^7 or R^8;

Each R^5 is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; haloalkyl; C1-C10 alkyl substituted with 1-3

independent aryl, R^7 or R^9 groups; C3-C10 cycloalkyl substituted with 1-3 independent aryl, R^7 or R^9 groups; or C2-C10 alkenyl substituted with 1-3 independent aryl, R^7 or R^9;

Each R^6 is independently $C(O)R^5$, $COOR^5$, $C(O)NR^5R^5$, $C(=N\ R^5)\ NR^5R^5$, or $S(O)_n\ R^5$;

Each R^7 is independently halo, CF_3, SR^{10}, OR^{10}, $OC(O)R^{10}$, $NR^{10}R^{10}$, $NR^{10}R^{11}$, $NR^{11}R^{11}$, $COOR^{10}$, NO_2, CN, $C(O)R^{10}$, $OC(O)NR^{10}R^{10}$, $C(O)NR^{10}R^{10}$, $N(R^{10})C(O)R^{10}$, $N(R^{10})(COOR^{10})$, $S(O)_nNR^{10}R^{10}$; $NR^{10}S(O)_nNR^{10}R^{10}$; $NR^{10}S(O)_nR^{10}$; or $P(O)(OR^5)_2$;

Each R^8 is independently a 3-8 membered monocyclic, 7-12 membered bicyclic, or 11-14 membered tricyclic ring system having 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2, 3 or 4 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; halo; sulfur; oxygen; CF_3; SR^5; OR^5; $OC(O)R^5$; NR^5R^5; NR^5R^6; NR^6R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)NR^5R^5$; $S(O)_nNR^5R^5$; $NR^5C(O)NR^5R^5$; $NR^5C(O)R^9$; $NR^5S(O)_nNR^5R^5$; $NR^5S(O)_nR^9$; C1-C10 alkyl substituted with 1-3 independent R^7, R^9 or aryl; or C2-C10 alkenyl substituted with 1-3 independent R^7, R^9 or aryl;

Each R^9 is independently a 3-8 membered monocyclic, 7-12 membered bicyclic, or 11-14 membered tricyclic ring system having 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; halo; sulfur; oxygen; CF_3; haloalkyl; SR^{10}; OR^{10}; $NR^{10}R^{10}$; $NR^{10}R^{11}$; $NR^{11}R^{11}$; $COOR^{10}$; NO_2; CN; $C(O)R^{10}$; $S(O)_nR^{10}$; $S(O)_nNR^{10}R^{10}$; or $C(O)NR^{10}R^{10}$;

Each R^{10} is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; haloalkyl; C1-C10 alkyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NR^{12}C(O)R^{12}$, $N(R^{12})(COOR^{12})$, $S(O)_nNR^{12}R^{12}$, or $OC(O)R^{12}$; or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-

C10 cycloalkenyl, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NR^{12}C(O)R^{12}$, $N(R^{12})(COOR^{12})$, $S(O)_nNR^{12}R^{12}$, or $OC(O)R^{12}$;

Each R^{11} is independently $C(O)R^{10}$, $COOR^{10}$, $C(O)NR^{10}R^{10}$ or $S(O)_nR^{10}$;

Each R^{12} is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl substituted with 1-3 independent C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NR^{13}C(O)R^{13}$, or $OC(O)R^{13}$; or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NR^{13}C(O)R^{13}$, or $OC(O)R^{13}$;

Each R^{13} is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl optionally substituted with halo, OR^{14}, SR^{14}, $NR^{14}R^{14}$, $COOR^{14}$, NO_2, CN; or phenyl optionally substituted with halo, CF_3, OR^{14}, SR^{14}, $NR^{14}R^{14}$, $COOR^{14}$, NO_2, CN;

Each R^{14} is independently H; C1-C10 alkyl; C3-C10 cycloalkyl or phenyl;

Each R^{16} is independently H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8; halo; haloalkyl; $COOR^5$; $C(O)R^5$; $C(O)C(O)R^5$; $C(O)NR^5R^5$; $S(O)_nR^5$; $S(O)_nNR^5R^5$; C1-C10 alkyl substituted with 1-3 independent aryl, R^7, R^8, or phenyl optionally substituted with substituted with 1-4 independent R^{23}; or C2-C10 alkenyl substituted with 1-3 independent aryl, R^7 or R^8;

Each R^{23} is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8; halo; haloalkyl; SR^5; OR^5; $OC(O)R^5$; NR^5R^5; NR^5R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)C(O)R^5$; $C(O)NR^5R^5$; $S(O)_nR^5$; $S(O)_nNR^5R^5$; $NR^5C(O)NR^5R^5$; $NR^5C(O)C(O)R^5$; $NR^5C(O)R^5$; $NR^5(COOR^5)$; $NR^5C(O)R^8$; $NR^5S(O)_nNR^5R^5$; $NR^5S(O)_nR^5$; $NR^5S(O)_nR^8$; $NR^5C(O)C(O)NR^5R^5$; $NR^5C(O)C(O)NR^5R^6$; $OC(O)NR^5R^5$; $OS(O)_nNR^5R^5$; $NR^5S(O)_nOR^5$; $P(O)(OR^5)_2$; C1-C10 alkyl substituted with 1-3 independent aryl, R^7 or R^8; or C2-C10 alkenyl substituted with 1-3 independent aryl, R^7 or R^8;

Each haloalkyl is independently a C1-C10 alkyl substituted with one or more halogen atoms, selected from F, Cl, Br, or I, including perhaloalkyl;

Each aryl is independently a 6-carbon monocyclic, 10-carbon bicyclic or 14-carbon tricyclic aromatic ring system optionally substituted with 1-3 independent C1-C10 alkyl;

C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; R^9; halo; haloalkyl; OR^{10}; SR^{10}; $NR^{10}R^{10}$; $NR^{10}R^{11}$; $COOR^{10}$; NO_2; CN; $C(O)R^{10}$; $C(O)C(O)R^{10}$; $C(O)NR^{10}R^{10}$; $N(R^{10})C(O)NR^{10}R^{10}$; $N(R^{10})C(O)R^{10}$; $N(R^{10})S(O)_nR^{10}$; $N(R^{10})(COOR^{10})$; $NR^{10}C(O)C(O)R^{10}$; $NR^{10}C(O)R^9$; $NR^{10}S(O)_nNR^{10}R^{10}$; $NR^{10}S(O)_nR^9$; $NR^{12}C(O)C(O)NR^{12}R^{12}$; $S(O)_nR^{10}$; $S(O)_nNR^{10}R^{10}$; $OC(O)R^{10}$; C1-C10 alkyl substituted with 1-3 independent R^9, halo, CF_3, OR^{10}, SR^{10}, $OC(O)R^{10}$, $NR^{11}R^{11}$, $NR^{10}R^{10}$, $NR^{10}R^{11}$, $COOR^{10}$, NO_2, CN, $C(O)R^{10}$, $OC(O)NR^{10}R^{10}$, $C(O)NR^{10}R^{10}$, $N(R^{10})C(O)R^{10}$, $N(R^{10})$ $(COOR^{10})$, $S(O)_nNR^{10}R^{10}$; R^{10}; or C2-C10 alkenyl substituted with 1-3 independent R^9, halo, CF_3, OR^{10}, SR^{10}, $OC(O)R^{10}$, $NR^{11}R^{11}$, $NR^{10}R^{10}$, $NR^{10}R^{11}$, $COOR^{10}$, NO_2, CN, $C(O)R^{10}$, $OC(O)NR^{10}R^{10}$, $C(O)NR^{10}R^{10}$, $N(R^{10})C(O)R^{10}$, $N(R^{10})$ $(COOR^{10})$, $S(O)_nNR^{10}R^{10}$;

Each heterocyclyl is independently a 3-8 membered nonaromatic monocyclic, 8-12 membered nonaromatic bicyclic, or 11-14 membered nonaromatic tricyclic, ring system having 1-4 heteroatoms if monocyclic, 1-8 heteroatoms if bicyclic, or 1-10 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S;

Each heteroaryl is independently a 5-8 membered aromatic monocyclic, 8-12 membered aromatic bicyclic, or 11-14 membered aromatic tricyclic ring system having 1-4 heteroatoms if monocyclic, 1-8 heteroatoms if bicyclic, or 1-10 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S;

provided R^1 and R^2 are not both 1-alkylpyridinium, or both 4-pyridyl **[or both morpholino]**;

further provided neither R^1 or R^2 is **[not]** morpholino or NH_2;

[further provided R^1 and R^2 are not both hydroxy, methoxy, ethoxy or phenoxy;

further provided R^1 is not phenoxy, acetylamino, or methylamino when R^2 is morpholino;

further provided R^1 is not methoxy or hydroxy when R^2 is 4-chlorophenylamino;

further provided R^1 is not phenoxy, methoxy or ethoxy when R^2 is 4-aminophenylsulfonylamino;

further provided R^1 is not phenoxy when R^2 is 4-methylthiophenylamino or sulfanilamido; and

further provided R^1 is not hydroxy when R^2 is hexylamino, phenylamino, 3-methylphenylamino, 2-ethoxyphenylamino, 4-methylthiophenylamino, 2-

ethylsulfinylphenylamino, 3-propylsulfonylphenylamino, 4-acetylphenylamino, 4-sulfamylphenylamino, 3-nitrophenylamino, 4-cyanophenylamino, 4-carboxyphenylamino, 4-(acetylamino)phenylamino, 4-biphenylamino, 1-naphthylamino, 4-pyridylamino, 2-thiazolylamino, 4-quinolylamino, and 2-pyrimidinylamino].

6. (Amended twice) The compound of claim 1 wherein,

R^1 is independently NHR^5;

R^2 is independently NHR^3;

Each R^3 is independently aryl; phenyl optionally substituted with 1-5 independent R^4 on each ring; or heteroaryl optionally substituted with 1-4 independent R^4 on each ring;

Each R^4 is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8; halo; CF_3; SR^5; OR^5; $OC(O)R^5$; NR^5R^5; NR^5R^6; NR^5R^{16}; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)C(O)R^5$; $C(O)NR^5R^5$; $S(O)_nR^5$; $S(O)_nNR^5R^5$; $NR^5C(O)NR^5R^5$; $NR^5C(O)C(O)R^5$; $NR^5C(O)R^5$; $NR^5(COOR^5)$; $NR^5C(O)R^8$; $NR^5S(O)_nNR^5R^5$; $NR^5S(O)_nR^5$; $NR^5S(O)_nR^8$; $NR^5C(O)C(O)NR^5R^5$; $NR^5C(O)C(O)NR^5R^6$; $OC(O)NR^5R^5$; $OS(O)_nNR^5R^5$; $NR^5S(O)_nOR^5$; $P(O)(OR^5)_2$; C1-C10 alkyl substituted with 1-3 independent aryl, R^7 or R^8; or C2-C10 alkenyl substituted with 1-3 independent aryl, R^7 or R^8;

Each R^5 is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; haloalkyl; C1-C10 alkyl substituted with 1-3 independent aryl, R^7 or R^9 groups; C3-C10 cycloalkyl substituted with 1-3 independent aryl, R^7 or R^9 groups; or C2-C10 alkenyl substituted with 1-3 independent aryl, R^7 or R^9;

Each R^6 is independently $C(O)R^5$, $COOR^5$, $C(O)NR^5R^5$, $C(=NR^5)NR^5R^5$, or $S(O)_nR^5$;

Each R^7 is independently halo, CF_3, SR^{10}, OR^{10}, $OC(O)R^{10}$, $NR^{10}R^{10}$, $NR^{10}R^{11}$, $NR^{11}R^{11}$, $COOR^{10}$, NO_2, CN, $C(O)R^{10}$, $OC(O)NR^{10}R^{10}$, $C(O)NR^{10}R^{10}$, $N(R^{10})C(O)R^{10}$, $N(R^{10})(COOR^{10})$, $S(O)_nNR^{10}R^{10}$; $NR^{10}S(O)_nNR^{10}R^{10}$; $NR^{10}S(O)_nR^{10}$; or $P(O)(OR^5)_2$;

Each R^8 is independently a 3-8 membered monocyclic, 7-12 membered bicyclic, or 11-14 membered tricyclic ring system having 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2, 3 or 4 atoms of each ring may be

substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; halo; sulfur; oxygen; CF_3; SR^5; OR^5; $OC(O)R^5$; NR^5R^5; NR^5R^6; NR^6R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)NR^5R^5$; $S(O)_nNR^5R^5$; $NR^5C(O)NR^5R^5$; $NR^5C(O)R^9$; $NR^5S(O)_nNR^5R^5$; $NR^5S(O)_nR^9$; C1-C10 alkyl substituted with 1-3 independent R^7, R^9 or aryl; or C2-C10 alkenyl substituted with 1-3 independent R^7, R^9 or aryl;

Each R^9 is independently a 3-8 membered monocyclic, 7-12 membered bicyclic, or 11-14 membered tricyclic ring system having 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; halo; sulfur; oxygen; CF_3; haloalkyl; SR^{10}; OR^{10}; $NR^{10}R^{10}$; $NR^{10}R^{11}$; $NR^{11}R^{11}$; $COOR^{10}$; NO_2; CN; $C(O)R^{10}$; $S(O)_nR^{10}$; $S(O)_nNR^{10}R^{10}$; or $C(O)NR^{10}R^{10}$;

Each R^{10} is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; haloalkyl; C1-C10 alkyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NR^{12}C(O)R^{12}$, $N(R^{12})(COOR^{12})$, $S(O)_nNR^{12}R^{12}$, or $OC(O)R^{12}$; or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NR^{12}C(O)R^{12}$, $N(R^{12})(COOR^{12})$, $S(O)_nNR^{12}R^{12}$, or $OC(O)R^{12}$;

Each R^{11} is independently $C(O)R^{10}$, $COOR^{10}$, $C(O)NR^{10}R^{10}$ or $S(O)_nR^{10}$;

Each R^{12} is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl substituted with 1-3 independent C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NR^{13}C(O)R^{13}$, or $OC(O)R^{13}$; or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NR^{13}C(O)R^{13}$, or $OC(O)R^{13}$;

Each R^{13} is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl optionally substituted with halo, OR^{14},

SR^{14}, $NR^{14}R^{14}$, $COOR^{14}$, NO_2, CN; or phenyl optionally substituted with halo, CF_3, OR^{14}, SR^{14}, $NR^{14}R^{14}$, $COOR^{14}$, NO_2, CN;

Each R^{14} is independently H; C1-C10 alkyl; C3-C10 cycloalkyl or phenyl;

Each R^{16} is independently H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8; halo; CF_3; $COOR^5$; $C(O)R^5$; $C(O)C(O)R^5$; $C(O)NR^5R^5$; $S(O)_nR^5$; $S(O)_nNR^5R^5$; C1-C10 alkyl substituted with 1-3 independent aryl, R^7, R^8, or phenyl optionally substituted with substituted with 1-4 independent R^{23}; or C2-C10 alkenyl substituted with 1-3 independent aryl, R^7 or R^8; and

Each R^{23} is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8; halo; CF_3; SR^5; OR^5; $OC(O)R^5$; NR^5R^5; NR^5R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)C(O)R^5$; $C(O)NR^5R^5$; $S(O)_nR^5$; $S(O)_nNR^5R^5$; $NR^5C(O)NR^5R^5$; $NR^5C(O)C(O)R^5$; $NR^5C(O)R^5$; $NR^5(COOR^5)$; $NR^5C(O)R^8$; $NR^5S(O)_nNR^5R^5$; $NR^5S(O)_nR^5$; $NR^5S(O)_nR^8$; $NR^5C(O)C(O)NR^5R^5$; $NR^5C(O)C(O)NR^5R^6$; $OC(O)NR^5R^5$; $OS(O)_nNR^5R^5$; $NR^5S(O)_nOR^5$; $P(O)(OR^5)_2$; C1-C10 alkyl substituted with 1-3 independent aryl, R^7 or R^8; or C2-C10 alkenyl substituted with 1-3 independent aryl, R^7 or R^8;

provided neither R^1 nor R^2 is **[not]** NH_2.

22. A composition comprising a compound of any of claims 1-7 and 10-21 **[1-21]** and a pharmaceutically acceptable carrier.

24. (Amended twice) A method of treating kinase-mediated disease or disease symptoms in a mammal comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21 **[1-21]**.

25. (Amended twice) A method of inhibiting kinase activity in a mammal comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21 **[1-21]**.

26. (Amended twice) A method of treating disease or disease symptoms in a mammal comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21 **[1-21]**.

27. (Amended twice) A method of inhibiting angiogenesis or vasculogenesis activity in a mammal comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21 **[1-21]**.

Add new Claims as follows:

--32. A method of treating cancer comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21.--

--33. A method of treating myeloproliferative disorders comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21.--

--34. A method of treating autoimmune disorders comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21.--

--35. A method of treating polycystic kidney disease comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21.--